Predictive and prognostic value of preoperative complete blood count in prostate cancer

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Abstract

Aim: The predictive and prognostic value of complete blood count (CBC) in different types of cancer has been frequently demonstrated in recent years. Prostate cancer is the second most common cancer in men worldwide and is one of the most leading causes of death. In our study, we sought to find out whether CBC parameters could distinguish patients with prostate cancer from patients with benign prostatic hyperplasia. Material and Method: Laboratory findings and histopathological findings of totally 93 patients were retrospectively re-evaluated. The absolute neutrophil count (ANC), the absolute lymphocyte count (ALC), platelet count, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and mean platelet volume (MPV) values were noted. In patients with prostate cancer, pathological parameters such as prostate weight, tumor percentage, Gleason score perineural invasion, seminal vesicle involvement, apical and radial margin involvement, extra-prostatic extension were determined. Results: In our study, we found that ANC, NLR, PLR, and MPV were significantly different between patients with benign prostatic hyperplasia and with prostate cancer ($p < 0.05$). We found that ANC and MPV were much more successful in discriminating these patients ($p < 0.001$). We have shown that ANC has higher specificity and MPV value has higher sensitivity. However, we didn't find any correlation between blood parameters and pathological parameters in patients with prostate cancer. Discussion: Our study has shown that ANC, NLR, PLR, and MPV have the ability to discriminate malignant lesions from benign lesions. Although no correlation with pathologic parameters can be determined, we think that CBC might be evaluated as an auxiliary tool for prostate cancer diagnosis.

Keywords

CBC; NLR; MPV; PLR; Prostate Cancer

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Introduction

Prostate cancer is the second most common cancer and one of the most leading causes of death in men worldwide [1]. By means of prostate-specific antigen (PSA) as a screening method showed that there has been a slight decrease in prostate cancer mortality in recent years [1]. However, it is no longer recommended to be used as a screening test due to overdiagnosis ranging from 23% - 42% of all prostate cancer by PSA [1,2]. For this reason, effective biomarkers in screening and diagnosis would be beneficial for avoiding unnecessary operations.

The predictive and prognostic value of complete blood count (CBC) has been manifested by recent studies. It has been known that there is an association between inflammation and cancer and the use of CBC is the subject of research because of its capability to show an inflammatory process in the early stages of diseases.

The results of CBC differ in cancer patients and give us some clues about the prognosis of the disease. This suggests that routine CBC may be used for different purposes such as cancer screening, diagnoses or follow-ups in the future.

In this study, we aimed to investigate whether CBC parameters differ between patients with prostate cancer (PCa) and those with a benign prostate hyperplasia (BPH). We also aimed to show the relationship between hematological parameters and pathological parameters with prognostic significance in cancer patients. There are limited studies in the literature comparing laboratory findings with all types of pathological findings in prostate cancer.

Material and Method

All procedures performed in the current study were approved by research ethics committee of Meram Medical Faculty of Necmettin Erbakan University (ID: 2018/1194) in accordance with the 1964 Helsinki Declaration and its later amendments. A total of 93 patients with PCa and 23 patients with BPH were enrolled in the study. Prostatectomy specimens evaluated in pathology department were retrospectively screened and patients' medical records were reviewed. Formal written informed consent was not required with a waiver by the appropriate national research ethics committee. We exclude the patients with other accompanying diseases, with an active infection or under the treatment of any type of infection at the time of the application and those with a diagnosis of prostatitis in the pathology report. The patients who had received any cancer treatment before the operation were also excluded from the study. Preoperative CBC results and postoperative pathology findings of the included patients were evaluated retrospectively. The absolute neutrophil count (ANC), absolute lymphocyte count (ALC), platelet value, and neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and mean platelet volume (MPV) values were noted in all patients. NLR was calculated by dividing the number of neutrophils to the number of lymphocytes and PLR was calculated by dividing the number of platelets to the number of lymphocytes. The results of the patients with PCa were compared to the results of patients with BPH. Any difference or relationship of these parameters was investigated between the patients with malignant and benign diseases. On histopathological examination, prognostic pathological parameters were evaluated such as prostate weight, tumor percentage, Gleason score, perineural invasion, seminal vesicle invasion, apical and radial margin involvement, tumor stage and extra-prostatic extension in cancer patients. Hematological parameters were compared with these pathological parameters and any correlation was investigated between them. Patients' medical records were also used to obtain the data on survival.

Statistical analysis was performed by using IBM SPSS for Windows Version 22.0. Numerical values were outlined by median ± standard deviation [Min - Max] values and categorical variables were outlined by the number and percentage. The Kolmogorov-Smirnov test was used to examine whether the numerical variables showed normal distribution. The similarity of group variances was investigated by the Levene's test. Mann-Whitney U test was used to investigate whether there was any difference in numerical variables between the two groups. Kruskal-Wallis test was used for comparison of more groups. The cut-off point for the values that distinguish prostate cancer and BPH groups were determined by ROC curve analysis. Sensitivity and selectivity values for the best cut off point were given. The area under the ROC curve is calculated. The significance level was taken as $p < 0.05$.

Results

In this study, data of 93 patients aged between 51 and 87 years obtained from pathological examination and laboratory investigations were evaluated. Seventy patients (75%) had PCa and 23 patients (25%) had BPH. After evaluation, we found that ANC and MPV in patients with PCa were significantly higher than those with BPH in our study ($p < 0.001$) (Table 1).

In addition to that, NLR and PLR values were found to be higher in patients with PCa compared to the patients with BPH. This difference was also statistically significant ($p < 0.05$) (Table 1). According to the ROC analysis, MPV was found to have 95% sensitivity but has low specificity. On the contrary, ANC was found to have lower sensitivity but higher specificity than MPV (Table 2).

Comparing the data obtained from CBC with the findings of the pathological evaluation, no significant relationship was found between hematological parameters and pathological parameters such as Gleason score, perineural invasion, apical and ra-

Table 1. Comparison of patients with prostate cancer and with benign prostatic hyperplasia.

	BPH (n=23) ($x10^3$µL)		PCa (n=70) ($x10^3$µL)		P value
	Mean ± SD	Median [Min-Max]	Mean ± SD	Median [Min-Max]	
ANC	4.92 ± 1.91	4.71 [2.78 - 9.74]	8.21 ± 4.73	7.11 [0.65 - 22.87]	<0.001*
ALC	3.33 ± 4.63	2.04 [0.09 - 22.4]	1.85 ± 1.44	1.61 [0.16 - 7.42]	0.059
NLR	5.26 ± 14.45	2.16 [0.12 - 71.3]	10.59 ± 13.67	3.91 [0.78 - 59.56]	0.002*
Platelet	221 ± 56.62	240 [102 - 331]	219.13 ± 70.04	214 [81 - 380]	0.493
PLR	230.47 ± 633	104.2 [0.98-3122.1]	250.41 ± 324.08	126.74 [40 - 1800]	0.023*
MPV	7.53 ± 1.22	7.19 [4.88 - 9.98]	8.77 ± 1.05	8.7 [6.5 - 11.6]	<0.001*

BPH: Benign Prostatic Hyperplasia; PCa: Prostate cancer; ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; NLR: Neutrophil lymphocyte ratio; PLR: Platelet lymphocyte ratio; MPV: Mean platelet volume; *Statistically significant

dial surgical margin involvement, seminal vesicle involvement, the presence of extraprostatic extension, tumor stage, and survival (Table 3 and Table 4). In addition, no correlation was found between tumor percentage and CBC results (Table 5). In our study, the longest follow-up period was 9 years and the

Table 2. Cut off points of laboratory parameters discriminating benign and malignant samples.

	Cut off point ($x10^3$µL)	AUC	p	Sensitivity	Specificity
ANC	>6.61	0.749	0.001*	0.571	0.870
ALC	<1.170	0.632	0.059	0.386	0.957
NLR	>3.25	0.714	0.002*	0.571	0.870
Platelet	<239.5	0.548	0.493	0.686	0.522
PLR	>144.28	0.658	0.023*	0.429	0.826
MPV	>7.285	0.780	0.001*	0.957	0.565

ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; NLR: Neutrophil lymphocyte ratio; PLR: Platelet lymphocyte ratio; MPV: Mean platelet volume;*Statistically significant

Table 3. Association between ANC, ALC, NLR and pathological parameters in prostate cancer patients.

Pathological parameters	ANC ($x10^3$µL)	P value	ALC ($x10^3$µL)	P value	NLR	P value
Gleason score						
2-6 (n=22)	8.42±6.02		1.9±1.92		11.08±14.51	
7 (n=35)	7.94±4.05	0.879	1.9±1.23	0.613	8.85±10.3	
8-10 (n=12)	8.47±4.44		1.63±1.07		15.21±20.17	0.882
Perineural invasion						
present (n=44)	8.06±4.36	0.789	1.89±1.25	0.316	8.95±11.27	
absent (n=26)	8.45±5.38		1.79±1.74		13.36±16.87	0.328
Apical margin involvement						
present (n=16)	7.66±4.04	0.727	1.31±1.01	0.095	15.99±17.56	
absent (n=54)	8.37±4.94		2.02±1.51		8.99±12.03	0.281
Radial margin involvement						
present (n=15)	6.22±3.09	0.109	1.33±0.93	0.15	9.13±10.72	
absent (n=55)	8.75±4.97		2±1.52		10.99±14.43	0.989
Extra-prostatic extension						
present (n=20)	8.58±4.36	0.467	1.59±0.98	0.687	10.83±12.49	
absent (n=50)	8.06±4.9		1.96±1.58		10.5±14.23	0.353
Seminal vesicle involvement						
present (n=20)	8.51±4.82	0.823	1.93±1.06	0.349	8.81±11.92	
absent (n=50)	8.12±4.74		1.83±1.54		11.12±14.21	0.727
Tumor stage						
T2 (n=48)	8.22±4.94	0.899	1.91±1.59	0.869	10.88±14.41	0.840
T3 (n=22)	8.18±4.35		1.72±1.04		9.97±12.2	
Survival						
alive (n=65)	8.29±4.7	0.293	1.88±1.46	0.642	10.45±13.39	0.877
dead (n=5)	7.07±5.49		1.48±1.07		12.43±18.67	

ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; NLR: Neutrophil to lymphocyte ratio

Table 4. Relationship between platelet count, PLR, and MPV and pathological parameters in prostate cancer patients.

Pathological parameter	Platelet ($x10^3$µL)	P value	PLR	P value	MPV (fL)	P value
Gleason score						
2-6 (n=22)	223.59±77.13		266.61±372.56		8.75±0.79	
7 (n=35)	219.29±70.23	0.956	221.46±272.44	0.554	8.75±1.24	
8-10 (n=12)	211.17±63.64		316.25±393.53		8.89±0.98	0.836
Perineural invasion						
present (n=44)	217.23±72.61	0.770	194.92±207.2	0.290	8.65±1.15	
absent (n=26)	222.35±66.72		344.32±448.82		8.96±0.85	0.181
Apical margin involvement						
present (n=16)	199.63±42.84	0.251	382.68±442.01	0.198	9.03±1.41	
absent (n=54)	224.91±75.61		211.22±273.11		8.69±0.92	0.405
Radial margin involvement						
present (n=15)	205.73±77.84	0.255	306.77±371.69	0.379	9.03±1.21	
absent (n=55)	222.78±68.07		235.04±311.86		8.7±1	0.352
Extra-prostatic extension						
present (n=20)	210.6±71.11	0.391	262.26±333.95	0.927	8.45±1.34	
absent (n=50)	222.54±70.03		245.67±323.37		8.9±0.89	0.075
Seminal vesicle involvement						
present (n=20)	233.94±65.1	0.291	207.6±215.04	0.595	8.35±1.3	
absent (n=50)	214.74±71.42		263.1±350.61		8.89±0.95	0.080
Tumor stage						
T2 (n=48)	221.65±71.36	0.635	252.62±328.31	0.667	8.89±0.91	
T3 (n=22)	213.64±68.36		245.59±322.2		8.49±1.29	0.108
Survival						
alive (n=65)	218.42±72.42	0.423	249.22±332.55	0.410	8.77±1.04	
dead (n=5)	228.4±24.06		265.88±204.87		8.7±1.34	0.842

PLR: Platelet to lymphocyte ratio; MPV: Mean platelet volume

Table 5. Correlation between tumor percentage and laboratory parameters.

	Tumor percentage	
	Correlation coefficient	p
ANC	0.127	0.295
ALC	0.077	0.528
NLR	0.029	0.810
Platelet	-0.070	0.562
PLR	-0.080	0.510
MPV	-0.123	0.311

ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; MPV: Mean platelet volume

average follow-up period was 6 years. Survival analysis cannot be performed because only five cancer patients lost their lives during the study period.

Discussion

In our study, we have shown that ANC, NLR, PLR, and MPV obtained from CBC can discriminate patients with PCa from the patients with BPH. We have found that ANC and MPV values are much more successful in differentiating these patients. We have also shown that ANC has a high selectivity and the MPV has a high sensitivity. However, we did not find any significant relationship between blood parameters and pathological parameters such as Gleason score, extraprostatic extension, perineural invasion, tumor stage, apical and radial surgical margin, seminal vesicle involvement.

The results of CBC, especially the systemic inflammatory parameters, contain many clues reflecting how the human mechanism works. They are very helpful in the diagnosis of many diseases in addition to the physical examination findings. Recent studies have shown that CBC findings might also be used in tumoral diseases. The relationship between inflammation and cancer has been already known for decades [3]. It has been known that some cancers develop on the ground of chronic inflammation or some infectious agents are involved in cancer etiology. However, during the cancer development, inflammatory mediators play an important role in creating a microenvironment that will allow the tumor to grow and spread [4]. Further, many studies suggest that not only the inflammatory response in the tumoral tissue but also the systemic inflammatory response is associated with the tumor prognosis [5]. Similar to the inflammatory cells, platelets play a role in the development of cancer [6]. Platelets also contribute to the formation of angiogenesis by stimulating vascular and endothelial growth factors, in turn supporting cancer development [5]. Moreover, platelets play an active role in the metastatic process by facilitating the adhesion of cells to the vessels [5]. The thrombocytosis has been shown to be also associated with advanced or metastatic cancers and regarded as a negative predictive marker for many cancers such as endometrial, cervical, ovarian, gastric, and esophageal carcinoma, and breast cancer [7].

In recent years, studies have been accumulated on the utility of routine CBC parameters for diagnosis, prognosis, and follow-up of cancer patients [7-12]. Among them, NLR is the most commonly used parameter. In the present study, we aimed to achieve a more comprehensive analysis by comparing not only NLR but also other parameters of CBC, such as ANC, ALC, platelet count, PLR, and MPV. In addition, in our study, we evaluated many pathological parameters since in most of the studies hematological parameters have been solely compared to the Gleason score.

NLR, the most studied parameter, has been reported to be associated with the advanced pathological stage and the lymph node involvement. It has been regarded as a predictive marker for biochemical recurrences [13]. Unlike many other studies, in the present study, we examined several pathological parameters. Unfortunately, we could not find any association between NLR and pathological parameters. This may be due to the limited number of patients enrolled in the study. Also, we could not evaluate biochemical recurrences due to the lack of follow-up data for all patients. In a recent study observing the availability of NLR in PCa cases, it was shown that NLR was not related to the Gleason score, surgical stage or surgical margin involvement. However, they suggested that a higher NLR ratio might be associated with a high Gleason score concluding that it might be a useful biomarker in the evaluation of low-risk patients [14]. In our study, there was no relation between many CBC parameters and the pathological parameters. In a meta-analysis study, it was shown that a higher NLR is associated with the lymph node involvement and poor survival, while not associated with the tumor stage and the Gleason score [15]. In recent studies, NLR has been also suggested to be a marker which should be used for tumor upgrading [16].

Similar to our study, Gökçe et al. [17] reported that NLR and ANC were significantly higher in patients with PCa compared to those with BPH. The authors reported a significant association between a higher Gleason score and a higher NLR. However, they examined only TRUS-guided core biopsies, and they evaluated neither the hematological nor the pathological parameters other than NLR and ANC. In the present study, we have examined the resection materials that allow us to evaluate prostate tissue completely. Therefore, we had more advantages than many other studies in terms of histological parameters. In our study, we found that increased ANC was helpful in differentiating the malignant disease from those benign ones. Similar to our results, a higher ANC has been reported to discriminate the malignant cases from the benign ones and to be related with the poorer prognosis [15-18].

In the study conducted by Kaynar et al. [19], NLR, PLR, and MPV values did not significantly differ between malignant and benign groups. However, we found that all three markers were significantly higher in the malignant lesions than in the benign ones even though we had a smaller number of patients. This can be explained by the fact that we did not enroll the patients with prostatitis into the benign group, unlike them. They also evaluated all types of prostate specimens, such as prostatectomy, biopsy, and transurethral resections. We included only open or radical prostatectomy cases and had a chance to exclude the cases with any possibility of an inflammation. They did not find any relation between the Gleason score and NLR or PLR values similar to our results.

MPV is an indicator of the thrombocyte activity and is related to the inflammatory conditions. In cancer patients, the role of MPV is not fully understood and controversial results have been reported in various studies. It was reported that a higher level of MPV has been found in patients with cancer in comparison to benign controls [20-24]. In the present study, we also found that patients with PCa had a significantly higher level of MPV compared to the patients with BPH. However, on the contrary to our findings, MPV was reported to be significantly lower in PCa than BPH in some studies [25]. We think that further investigations are required to clarify different MPV results.

We found that a higher PLR indicates the malignant disease, but we did not find any association with the pathological parameters. Similar to the present study, in the literature, a higher PLR has been found in cancer patients and also reported to predict shorter overall survival in prostate cancer [17].

The mean follow-up period of our study was 6 years. Only five patients with PCa lost their lives during the follow-up period. Therefore, we could not make survival analysis. We believe that further studies with longer follow-up periods will better demonstrate the prognostic value of ANC, NLR, PLR, and MPV.

Conclusions

In conclusion, ANC, MPV, NLR and PLR values have the ability to discriminate malignant lesions from benign lesions. These parameters might be used as an adjunct tool suggesting malignancy together with the other findings. Yet, further studies are needed to be carried out to assure the prognostic values of these parameters in prostate cancer patients with longer follow-up periods.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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